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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/045,970	01/11/2002	Rami Lidor-Hadas	1662/55602	3018

26646 7590 11/02/2006

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EXAMINER	
STOCKTON, LAURA LYNNE	
ART UNIT	**PAPER NUMBER**
1626	

DATE MAILED: 11/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/045,970	LIDOR-HADAS ET AL.	
	Examiner	Art Unit	
	Laura L. Stockton, Ph.D.	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 42-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 42-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-3 and 42-50 are pending in the application.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 18, 2006 has been entered.

Election/Restrictions

Applicants' election without traverse of Group I in Paper No. 7 was acknowledged in a previous Office

Action. The requirement was deemed proper and made FINAL in a previous Office Action.

Rejections made in the previous Office Action that do not appear below have been overcome by Applicants' amendments to the claims. Therefore, arguments pertaining to these rejections will not be addressed.

Response to Amendment

The Declaration under 37 CFR 1.132 filed February 17, 2005 is insufficient to overcome the rejection of claims 1-3 and 42-50 based upon obviousness under 35 USC § 103 over Chen {Zhongguo Yiyao Gongye Zazhi (1993), 24(6), pages 241-242}, Tyers {U.S. Pat. 4,845,115}, Coates et al. {U.S. Pat. 4,695,578} and Tyers {U.S. Pat. 4,835,173} as set forth in the last Office action because: (1) the Declaration

states, not shows, that the prior art does not have a purity of at least about 99.0%, see paragraph 2 on page 1; (2) the Declaration states that the product produced in Coates et al. has 0.12% of the exo-methylene whereas Applicants' claim that their product has less than about 0.1% of the exo-methylene in claim 51, which reads of Coates et al.'s 0.12%, see paragraph 3 of Declaration and instant claim 51; (3) the Declaration fails to show that the instant claimed product has a viable unexpected, unobvious and superior property, not just of allegedly higher purity; and (4) the Declaration is unclear if the cited prior art were compared with the instant claimed invention, see Table 3, for example.

Further, claims 42-50 are product-by-process claims. "Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its

method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). Also see M.P.E.P. 2113.

Since no other ingredient than the Ondansetron hydrochloride dihydrate is present in the pharmaceutical formulation, claims 45-47 and 50 are interpreted as compound claims.

Claim Objections

Claims 45-47 and 50 are objected to for being substantial duplicates of claims 42-44 and 48, respectively. When two claims in an application are duplicates, or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to

reject the other as being a substantial duplicate of the allowed claim. M.P.E.P. §706.03(k).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3 and 42-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen {Zhongguo Yiyao Gongye Zazhi (1993), 24(6), pages 241-242}, Tyers {U.S. Pat. 4,845,115}, Coates et al. {U.S. Pat. 4,695,578}, Tyers {U.S. Pat. 4,835,173} and Lidor-Hadas et al. {WO 02/36558}, each taken alone or in combination with each other when similar utilities are asserted. An English translation of Chen was provided

with a previous Office Action and will be referred to hereinafter.

Determination of the scope and content of the prior art (MPEP §2141.01)

Applicant claims Ondansetron hydrochloride dihydrate. Each of Chen {page 1, Compound (1) and page 2- section III}, Tyers '115 {column 3 and especially Example 2 in column 3}, Coates et al. {column 4 and especially Example 10 in column 20}, Tyers '173 {column 3 and especially Example 2 in column 3} and Lidor-Hadas et al. {page 3, lines 12-21 - Form A} teach Ondansetron hydrochloride dihydrate.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant claimed invention and the prior art is that the prior art is silent as to the purity of the product obtained.

Finding of prima facie obviousness--rational and motivation (MPEP §2142-2413)

It has long been the practice in the chemical and pharmaceutical arts to produce compounds in the form of crystals to secure a pure product. *In re Weijlard*, 69 U.S.P.Q. 86, 87 (C.C.P.A. 1946).

Changing the form, purity, color, or other characteristic of an old product without a new use as a result thereof does not render product patentable where utility remains the same. *Ex parte Hartop*, 139 USPQ 525. The compounds are of the same identical formula and as such would be expected to have the same utility. The difference, if any, may reside in there being of a higher purity.

One of ordinary skill in the art would be motivated to prepare a purer form of a known organic pharmaceutically active compound in the expectation of obtaining that very compound but with enhanced properties, e.g. improved solubility, shelf-life,

improved mode of administering properties, etc. In the absence of a showing of a viable unexpected, unobvious and superior property (not just an alleged higher purity), the instant claimed invention is found obvious over the cited prior art.

Response to Arguments

Applicant's arguments filed August 18, 2006 have been fully considered. Applicant argues that the consistent criterion for determination of obviousness is whether the prior art would have suggested to one of ordinary skill in the art that claimed subject matter should be carried out and would have a reasonable likelihood of success. Applicant argues that in order to form a proper basis for a rejection under 35 USC § 103, the prior art must provide some suggestion, either explicit or implicit, of the combination that allegedly renders claimed invention obvious. Applicant argues

that the Examiner's conclusionary statements do not adequately address the issue of motivation to combine.

Applicant's arguments have been considered but have not been found persuasive. Each of the cited prior art references teach Ondansetron hydrochloride dihydrate and each teach various uses for Ondansetron hydrochloride dihydrate such as treating or relieving nausea, migraines, psychotic disorders (i.e., schizophrenia), depression, cognitive disorders (i.e., dementia), etc. All of the cited prior art, except Chen, teach a recrystallization step when preparing the Ondansetron hydrochloride dihydrate. Since recrystallization is a known process for purifying a compound (see Grant & Hackh's Chemical Dictionary Fifth Edition, McGraw-Hill Book Company, New York, (1987), page 499), one skilled in the art would expect the obtained product to be of a high purity. One of ordinary skill in the art would be motivated to prepare a purer form of a known pharmaceutically active

compound in the expectation of obtaining that very compound but with enhanced properties, e.g. improved solubility, shelf-life, improved mode of administering properties, etc.

Applicant argues the decisions in *In re Deuel*, 51 F.3d 1552, 1558, 34 U.S.P.Q.2d 1210 (Fed. Cir. 1995); *In re Seaborg*, 382 F.2d 996, 997 (C.C.P.A. 1964); *In re Bergstrom*, 427 F.2d 1394, 1402 (C.C.P.A. 1970) and *In re Cofer*, 354 F.2d 664, 667 (C.C.P.A. 1966).

In response, the decisions have been considered. In *In re Deuel*, as stated by Applicant, the claimed compounds were not isolated in the prior art. In the cited prior art of the instant application, the cited prior art had isolated Ondansetron hydrochloride dihydrate and recrystallized the compound to obtain a purer product. Since a pure form of Ondansetron hydrochloride dihydrate has been prepared and is known in the art and is being administered to humans, the decision in *In re Seaborg* is not persuasive to the

instant fact situation. In *In re Bergstrom*, the question of patentability was under 35 U.S.C. 101 not 35 U.S.C. 103 since a rejection under 35 U.S.C. 103 had not been made in that case. In *In re Cofer*, the Court did state that consideration of the same usefulness is one consideration in the determination of a rejection under 35 U.S.C. 103. Another consideration the Court stated was if the prior art suggest the particular structure or form. The instant cited prior art does suggest making a purer form of Ondansetron hydrochloride dihydrate by the product undergoing a recrystallization step.

Applicant argues that: (1) the cited art does not disclose or suggest either explicitly or inherently the purity of the compound recited in the claims; (2) the Zhongguo (Chen) reference does not mention purity; (3) Example 2 of the '115 patent (Tyers) discloses a method of making Ondansetron hydrochloride dihydrate and recrystallization but does not disclose the purity of

Ondansetron hydrochloride dihydrate or the presence of exo-methylene; (4) Example 10 of the '578 patent (Coates et al.) discloses verbatim the method of making Ondansetron hydrochloride dihydrate as Example 2 in the '115 patent (Tyers); (5) the WO '558 publication (Lidor-Hadas et al.) discloses the methods of making Ondansetron hydrochloride dehydrate but does not disclose the purity; (6) the Declaration under 37 C.F.R. 1.132 demonstrates that the prior art was unable to obtain the recited purity; (7) an "obvious to try" argument has been applied without pointing out where the cited references would suggest such motivation; and (8) hindsight analysis has also been applied.

All of Applicant's arguments have been considered but have not been found persuasive. Applicant claims Ondansetron hydrochloride dihydrate. Each of Chen {page 1, Compound (1) and page 2- section III}, Tyers '115 {column 3 and especially Example 2 in column 3}, Coates et al. {column 4 and especially Example 10 in

column 20}, Tyers '173 {column 3 and especially Example 2 in column 3} and Lidor-Hadas et al. {page 3, lines 12-21 - Form A} teach Ondansetron hydrochloride dihydrate. The difference between the instant claimed invention and the prior art is that the prior art is silent as to the purity of the product obtained.

As previously stated, all of the cited prior art, except Chen, teach a recrystallization step when preparing the Ondansetron hydrochloride dihydrate. Since recrystallization is a known process for purifying a compound (see Grant & Hackh's Chemical Dictionary Fifth Edition, McGraw-Hill Book Company, New York, (1987), page 499), one skilled in the art would expect the obtained product to be of a high purity. One skilled in the art would also be motivated to make a purer product since the prior art teaches by their recrystallization step that a purer product is desired. It has long been the practice in the chemical and pharmaceutical arts to produce pure compounds since a

compound such as Ondansetron hydrochloride dihydrate, which is already known to one skilled in the pharmaceutical art to treat, for example, depression, would be administered orally, transdermally, etc. Purer forms of known products may be patentable, but the mere purity of a product, by itself, does not render the product unobvious. *Ex parte Gray*, 10 USPQ2d 1922 (Bd. Pat. App. & Inter. 1989). The showing in Declaration under 37 CFR 1.132 filed February 17, 2005 was found insufficient for reasons stated above.

Applicant argues that the Examiner has applied an "obvious to try standard." An "obvious to try" standard is deemed impermissible in two situations: 1) where the prior art gives no indication as to which of numerous parameters are critical, or gives no indication as to which of many possible choices is likely to be successful; and 2) where the prior art gives only general guidance with respect to the form of the invention, but not how to achieve it in new areas

of technology or in fields of experimentation which are only seemingly promising. *In re O'Farrell* 7 U.S.P.Q.2d 1673, 1681 (Fed. Cir. 1988). Because all of the cited prior art, except Chen, teach a recrystallization step when preparing the Ondansetron hydrochloride dihydrate, the instant rejection under 35 U.S.C. § 103 is not based on the improper "obvious to try" standard adopted by the Federal Circuit as set forth in *O'Farrell*.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Therefore, each of the cited prior art either taken alone, or in combination with each other, would make obvious the instant claimed invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura L. Stockton whose telephone number is (571) 272-0710. The examiner can normally be reached on Monday-Friday from 6:15 am to 2:45 pm. If the examiner is out of the Office, the examiner's supervisor, Joseph McKane, can be reached on (571) 272-0699.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

The Official fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

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October 30, 2006